

LOCKE (F.S.)

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POLARIZATION OF VERTEBRATE
VOLUNTARY MUSCLE

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OF THE ACTION OF ETHER ON CONTRACTURE AND OF POSITIVE KATHODIC POLARIZATION OF VERTEBRATE VOLUNTARY MUSCLE.

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PLATES XXVII-XXX.

By reasons which will be discussed in a later part of this paper and because it seemed that the action of such a substance would be of interest in connection with the study of contracture, I have been led to investigate the effect of ether on the form of contraction in response to a single stimulus of muscles which have been exposed to the influence of veratrine, of 0.6-per-cent sodium-chloride solution, and of dehydration. The effect of all these is to change the simple twitch of a normal muscle into a contraction enormously increased in amount and duration. Is the altered condition of the muscle, of which this abnormal form of response to a single stimulus is the outward and visible sign, stable as long as contractility persists under etherization, or is there associated with the gradual loss of contractility a change in the form of its expression—a return to the normal twitch of short duration?

I. THE ACTION OF ETHER ON VERATRINIZED MUSCLES.

GENERAL CONSIDERATIONS REGARDING METHOD.

Since, as has long been known, stimulation frequently repeated has itself an effect on the form of contraction of veratrinized muscle, it is evident that the intervals between successive stimuli must be long enough to exclude this source of error. On the other hand, in order to obtain a correct idea of the action of ether upon the form of

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contraction, it is highly necessary to apply as many stimulations to the muscle as possible before its contractility is extinguished by this substance. Preliminary experiments showed that intervals of not less than one minute are required to prevent too rapid falling away of the contracture. It is evident that, on account of this falling away, observations made during the muscle's recovery from etherization, regular stimulation being kept up through the whole experiment, are more convincing of an action of ether on the form of contraction than those made while the muscle is being etherized.

In the first experiments made the curarized and veratrinized sartorius muscle was etherized in various relatively small moist chambers, while induction shocks were passed at regular intervals through it from end to end through the bones with which it is in connection. Under these circumstances it was found that loss of contractility took place too speedily for the changes in the form of contraction of the muscle to be made out, if the necessary interval between successive stimulations was observed. Remembering, however, that a sartorius immersed in 0.6-per-cent sodium-chloride solution is acted on more readily at its tibial than at its pelvic end,* it occurred to me that under the action of ether both ends might become sooner unirritable than the rest of the muscle, and cause a "*polares Versagen*"—a failure of induction shocks sent through the muscle to stimulate it, owing to the local inexcitability of physiological kathode, perhaps also of anode. To avoid this, two electrodes of fine copper wire were made to lightly clip the muscle at the ends of its middle third. When the muscle was stimulated through these it was found to respond long enough to stimulation when etherized for the action of the vapour on the form of contraction to be made out.

I convinced myself directly by special experiments on the un-veratrinized curarized sartorius, subjected to the action of ether vapour and stimulated by induction shocks sent in both directions through its whole length and through its middle third, that the ends lose their excitability first, and that we have results corresponding exactly with

* F. S. Locke, Die Wirkung der physiologischen Kochsalzlösung auf quergestreifte Muskeln. *Arch. f. d. ges. Physiol.*, liv, 501, 1893.

those obtained with a 0.1-per-cent solution of potassium chloride on the muscle in question,* the tibial end being the more readily acted upon by the ether than the pelvic end. As etherization proceeds, the normally higher contractions called forth by induction shocks descending from pelvic to tibial end in the muscle become lower than those called forth by ascending shocks, the effect of the greater current density at the slender tibial end being annulled. As etherization proceeds, the contractions called forth by descending shocks continue to decrease in height more rapidly than those called forth by ascending shocks, and are the first to cease to appear. Ascending shocks from end to end become next ineffective, the continuity of the muscle remaining irritable for from two to three minutes after this occurs. It may be added that if the muscle is allowed to recover from the action of the ether, ascending shocks become effective sooner than the descending shocks, the latter, however, after recovery is complete, becoming once again the more effective.

In these experiments on curarized muscles I uniformly found the muscle much more excitable to shocks sent through its middle third than to shocks, even when descending, passed through its whole length. This result is readily explained by the lower electric excitability of the nerveless ends of the sartorius even when curarized—a fact established by Kuehne† and Pollitzer‡—and by the greater electric resistance of the whole muscle, with its tendons and stumps of bone left attached to them.

This difference of resistance was of course not present in the experiments of Kuehne and Pollitzer, in which the excitability of the muscle at different points of its length was investigated with induction shocks

* F. S. Locke, *op. cit.*, p. 510. The action of 0.1-per-cent potassium-chloride solution there described was due not merely to the potassium chloride, but also to the hypotonicity of the solution, causing it to act to a very high degree like pure water. This, fortunately, does not vitiate the demonstration by the help of this solution that the thinner tibial end of the sartorius is more susceptible than the pelvic end to the influence of media surrounding the muscle.

† Kuehne, *Arch. f. Anat., Physiol. u. wissenschaft. Med.*, 1860, 477.

‡ Pollitzer, *Journ. of Physiol.*, vii, 274, 1886.

passed obliquely through it by means of transverse wire electrodes placed a short distance apart, one on each side of the muscle. It may be pointed out here, however, that the conclusion drawn by Pollitzer from his results, that curare leaves unaffected certain nerve elements in the muscle, can not be well founded. He supposes that the excitation of these nerve elements ("the parts peripheral to the last node of Ranvier") explains the greater excitability of the parts of the muscle containing such. But, if this were the case, these nerve elements would be also excitable in a curarized muscle by currents passed through its whole length, and it would be as impossible for injury of the ends of such a muscle to render it inexcitable to currents entering and leaving it through injured tissue ("*polares Versagen*," Biedermann, Engelmann, and van Loon), as it actually is in the case of uncurarized muscles (van Loon). The failure of electric excitation caused by merely polar injury of a curarized muscle is to me the absolute proof that curare does not leave in physiological connection with the contractile material any excitable structures that do not traverse the muscle uninterruptedly from end to end. It is therefore, I think, the strongest possible proof of the independent irritability of muscle, as an argument for which I do not know it to have yet been used, and the results obtained by the electrical stimulation of curarized muscles described in this paper may be safely regarded as due to the action of the stimulus on muscle and on muscle alone.

My ultimate mode of experiment was as follows: The sartorius of a completely curarized grass-frog, into the dorsal lymph sac of which a few drops of a one-per-cent solution of veratrine acetate had been injected from six to fifteen minutes before the preparation of the muscle, was fixed in the muscle-chamber,* and the electrodes of fine copper wire were placed upon it. The muscle was first minimally stimulated, and was always found to give minimal contractions

* The chamber used is illustrated in the Cambridge Scientific Instrument Co.'s catalogue (p. 75, 1891), and measures approximately $12 \times 9 \times 6.5$ centimetres. It had been somewhat modified, and an ivory pulley 6 millimetres in diameter was fixed to the axis of the muscle lever, around which the thread carrying the load was slung. The distance between the axis and point of pull of the muscle was 40.5 millimetres; the length of the whole lever, 148 millimetres. The weight of the whole lever, with all its attachments except the actual load, was 1.05 gramme. When horizontal, it exercised a traction downward of 0.8 gramme along the thread connecting it with the muscle.

of long duration (Plate XXVII, Figs. 1A and 3A). The secondary coil of the inductorium was then moved up toward the primary, and regular stimulation with opening shocks commenced. The length of the interval between successive shocks was determined by the time of rotation of the drum, which in different experiments varied from one to three minutes. The successive curves of contraction were either superposed, in which case closing and opening of the primary circuit was effected by the passage through a mercury meniscus of an amalgamated copper wire rotating with the drum (the closing shocks were cut out by an *Abblender*), or followed one another in *imbrication latérale*, in which case closing and opening were effected by hand. After three or four typical veratrine curves had been recorded, a small piece of folded lint, on which about a cubic centimetre of ether had been poured, was placed in the moist chamber, and allowed to remain there until the muscle's irritability was sufficiently diminished. After its removal, the cover of the moist chamber before being replaced was well washed out with tap-water to get rid of ether clinging to it, the periodical stimulation being kept up as long as appeared necessary.*

THE ACTION OF ETHER ON THE FORM OF CONTRACTION OF VERATRINIZED MUSCLE.

There is no necessity to describe here the well-known general features of the action of veratrine on voluntary muscle. I will only draw special attention to the character of the contraction curves of the fresh veratrinized sartorius, which show that, contrary to the

* It is not always unavoidably necessary to send the stimulating shocks only through the middle third of the muscle in order to show clearly the effect of etherization on the veratrinized sartorius. This is occasionally possible, as I have found since the above was written, with the shocks sent from end to end of the muscle in the ordinary way. This result is accounted for by the fact that, as was found in the experiments made in the manner described in the text, muscles are occasionally met with which are very refractory to ether, and remain well irritable in an atmosphere saturated with it for as long as fifteen minutes. To avoid loss of time and material it is, however, advisable to take advantage of the difference in behaviour of the ends and of the continuity of the muscle above described.

opinion usually held, the action of the poison is by no means principally exerted during the period of relaxation of the muscle, the period of shortening being but little affected, but that the latter is also markedly modified, the amount of shortening being enormously increased, so that this phase of the contraction resembles that of a maximal tetanus rather than that of a normal twitch in answer to a single stimulation. It must be added, also, that the contraction curves of the fresh veratrinized sartorius stimulated at sufficiently long intervals show none or but slight traces of the characteristic and well-known dicrotism.

The action of ether on the form of contraction of veratrinized muscle is shown so clearly in the curves accompanying this paper that the verbal description of it will be made as short as possible.

The progressive diminution in the height of the contraction, which takes place under etherization, is accompanied also by an alteration in its form. A beginning of this is usually visible in the first contraction of the muscle after etherization has been begun, its summit being sharper and relaxation more rapid. The next contraction may be an almost normal twitch, followed only by a slight contraction-remainder. If, however, etherization be not so rapid, or the muscle be more profoundly veratrinized, the changes in the form of contraction may not be so abrupt, and the transitional forms from spasm to twitch are seen to be of the dicrotic type, the further action of the ether being especially exerted on their second summit, converting it into a mere contraction-remainder, which at last becomes minimal and succeeds a normal twitch.

The more profoundly the muscle has been veratrinized the more must the action of the ether be pushed before the effect of the veratrine is annulled, the simple twitches then obtained not being of great height. They are always, however, absolutely different in character from the prolonged minimal contractions evolved by minimal stimulation at the commencement or during the course of the experiment before etherization has been begun.

If etherization be put an end to when the stage of the simple twitch has been reached, the contraction curves of the muscle during

its gradual recovery of contractility are generally more instructive than those recorded during etherization. In successive contractions the contraction-remainder becomes greater and greater, while the duration of maximal contraction is usually more and more prolonged. The contraction-remainder may change into a secondary hump, which rises higher and higher till it overtops the initial shortening from which it is separated by the characteristic notch. In other cases, especially those of slightly veratrinized muscles, the notch may not be so manifest.

The effect of veratrine on the form of contraction never again becomes so marked as it was before etherization of the muscle. This is principally due to the effect of the repeated stimulation, and not to an after-effect of the ether—a fact which was proved by control experiments in which veratrinized muscles without being etherized were periodically stimulated in a similar manner. The same effect of repeated stimulation comes out in the etherization experiments if sufficiently prolonged, the veratrine spasms continuously decreasing after the maximum of recovery from ether has been reached. The etherization, if it has not been pushed too far, has but little permanent bad effect on a muscle, which, if allowed to remain after a first experiment for from thirty to forty-five minutes in Ringer's solution, shows once more the action of veratrine markedly, and can be used for a second etherization.

If the etherization has been too profound, the muscle may recover only imperfectly from it, to the extent of giving poor simple twitches, the veratrine effect not reappearing.

II. THE ACTION OF ETHER ON MUSCLES UNDER THE INFLUENCE OF PHYSIOLOGICAL SALT SOLUTION.

I have already described * the alterations of the normal form of contractions of voluntary muscle brought about by the treatment of it with 0.6-per-cent sodium-chloride solution. These are essentially similar to those caused by veratrine, the differences being of degree

* Locke, *Arch. f. d. ges. Physiol.*, liv, 501, 1893.

and not of kind. The relaxation from the state of spasm following a single stimulation is, in the case of the muscle treated with salt solution, usually more rapid than that of the veratrinized muscle. The only addition I will now make to my previous account is that, using chemically pure salt-solution in fairly large amount (100 cubic centimetres) in which to immerse the curarized or uncurarized sartorius muscle, I find that the condition of the frog has by no means the importance which I found it to possess in my earlier work. With good or poor muscles the spasm-conditioning action of the solution is well marked at all seasons of the year.

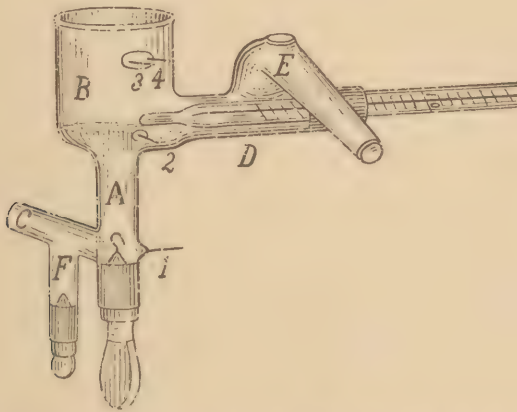
METHOD.

For the purpose of examining the action of ether on the form of contraction of muscles under the influence of physiological salt solution I have not etherized the muscle in a moist chamber, after an immersion in salt solution for from ten to thirty minutes, but have made use of a method which I have now long employed for the investigation of the action of various solutions on voluntary muscle, and which, on account of its convenience and general utility, will here be briefly described.

The objects of the method are to obtain a graphic record, as perfect as possible, of the contractions, weak and strong, of a sartorius muscle exposed to the action of a large quantity of fluid, the nature and temperature of which can be readily varied, and to enable one, with the help of only ordinary appliances, to strongly stimulate electrically the muscle without removing it from the fluid surrounding it. The use of a muscle-chamber of peculiar construction renders these objects easily attainable.

The muscle-chamber, shown in the figure (p. 638) two thirds its real size, is blown from glass tubing, and may be described as consisting essentially of a tube of varying calibre, the lower part of which (A) is of small (7.5 millimetres) diameter, to enable sufficient density of electric current to be readily obtained in the muscle, surrounded as it is by the fluid contained in the tube. The upper part (B) is of much larger (22 millimetres) diameter, in order to allow a certain amount of lateral play to the thread

connecting the muscle with the recording lever above it, so that there will be no risk that the thread will be drawn to and fixed, as far as the transmission of the movements of a lightly loaded muscle is concerned, in the edge of the fluid's meniscus. The muscle-chamber is closed below with a glass stopper, not ground in, but made to fit securely by means of a bit of rubber tubing of suitable size forming a packing between stopper and tube. A platinum hook attached to the stopper fixes the muscle in the way described below. Just above the stopper a side tube (C) acts as inlet for the slow stream of fluid maintained through the muscle-chamber. This flows out through the side tube attached to the upper part of the chamber (D), past the bulb of a thermometer fixed in this tube by a collar of rubber tubing, and then away through the bent tube (E), a hole blown at the top



of the bend of which prevents siphoning off. The bulb of the thermometer, which projects a little into the chamber, thus always remains under the surface of the fluid surrounding the muscle. The platinum electrodes 1 and 2 are used for direct stimulation; the platinum electrodes 3 and 4 for indirect stimulation. The latter are just above the surface of the fluid in the chamber. The tube F, usually closed by a rubber and glass stopper, serves to empty the chamber of fluid when required.

The sartorius is prepared for experiment in the following way: A fine silk ligature having been tied to its tibial tendon, and the muscle having been dissected out in connection with its half of the pelvic symphysis, the margin of the latter, except where the muscle is attached, is cut away so that but little more than the acetabulum is

left, and through the cartilaginous centre of this a hole is bored with a needle or pin. Through this hole the platinum hook fixed in the stopper closing the lower end of the muscle-chamber is passed, and, suspended by this, the muscle is allowed to hang down. A small pair of bulldog forceps is attached to the silk thread, its weight rendering easy the introduction of the muscle into its inverted chamber.

The chamber is now fixed in a small clamp underneath the recording lever, which consists of half a split straw attached to a Cambridge Scientific Instrument Company's "adjustable lever support," to the axis of which a small ivory pulley has been fixed, round which is slung a weight so as to counterpoise the lever. This method of counterpoising the lever has for advantages over the use of an elastic thread ease and permanency of adjustment.

The inlet tube of the chamber is connected by rubber tubing and branched glass tubing with three aspirating bottles, one of which contains Ringer's solution, another pure salt-solution (0.6 per cent), and the third pure salt-solution to which one or two per cent of ether has been added. The muscle is first stimulated when surrounded by Ringer's solution. Then a slow stream of pure salt-solution is established, and after the muscle has been exposed to its action a sufficient length of time for the alteration in the form of contraction to be marked, stimulation with strong opening induction shocks at constant intervals is commenced and maintained, a stream of ether-containing salt-solution being substituted for the other whenever it is thought necessary. The time at which the solution is turned on or off does not, of course, coincide with the change of solution in the muscle-chamber, which takes place a little later at a time not accurately determined and dependent on the rate of flow.

THE ACTION OF ETHER ON MUSCLES UNDER THE INFLUENCE OF PHYSIOLOGICAL SALT SOLUTION.

If, in the apparatus described, the sartorius muscle, curarized or uncurarized, and as lightly loaded as possible, be surrounded with Ringer's solution or with 0.6 per-cent salt-solution made with New River tap-water, in the vast majority of cases, especially if the tem-

perature of this solution be not too high—i. e., above 20° C.—it remains absolutely quiet, and when stimulated gives a simple twitch of short duration, not leaving behind it a contraction-remainder. But if a slow stream of pure 0.6-per-cent salt-solution be passed through the muscle-chamber, after a short but variable time the muscle begins to contract without further stimulation in the manner which Ringer * has already described. If five to fifteen minutes after the stream of pure salt-solution has been begun the muscle be electrically stimulated as before, it responds not with a twitch but with a spasm, more or less prolonged, and more or less irregular in character (Plate XXVIII, Figs. 4 and 5B). In many cases the “spontaneous” contractions appear to be superposed on the response to electrical stimulation. This need not be described further here.

More or less similar spasms appear in answer to further stimulations at constant intervals, while between them the spontaneous contractions break the abscissa. If now salt-solution containing ether (one to two per cent) be substituted for the pure normal salt-solution before employed, the first effect is seen to be a dying away of the “spontaneous” contractions, and loss of the tonic shortening of the muscle associated with them. The writing point now draws an unbroken line, and the next electrical stimulus calls forth usually only a simple twitch, the relaxation after which is complete.

Further action of the ether-containing salt-solution produces a lessening of the contractions due to electrical stimulation. If now the etherization be discontinued and a return be made to pure salt-solution, after some time both spontaneous contractions and spasms in answer to electrical stimulation return, but usually not to so great a degree as before etherization.

The spasm on electrical stimulation of the muscle due to salt-solution yields much more easily to etherization than that due to veratrine. The contractility of the muscle is very little affected at the time when it no longer gives spasmodic contractions. Its contractility may, in fact, be still increased when compared with that exhibited by the muscle when surrounded by Ringer's solution.

* Ringer, *Journ. of Physiol.*, vii, 291, 1886.

The above general description holds good for the majority of experiments conducted in the way described. In certain experiments, however, made in very cold weather, I found that 0.6-per-cent sodium-chloride solution acting on curarized sartorius muscles brought about extremely well-marked contractures, but had hardly any chemically stimulating action, whereas both kinds of effects were as usual produced on non-curarized muscles. This fact indicated that the "spontaneous" twitching of the muscles in the solution was brought about, at any rate at low temperatures, more especially by the action of the solution on the nerve endings, while its action on muscle itself was responsible for contracture. This supposition was supported by the few experiments I was able to make at higher temperatures with curarized muscles acted on by 0.6-per-cent sodium-chloride solution, containing 0.02-per-cent curare, to prevent the washing out of the poison from the nerve endings (Fig. 5). As, however, Ringer* concluded from his experiments with curare that the chemically stimulating action of salt solution is exerted on muscle itself, I do not care at this time to draw definite conclusions from my available material.

I will add here, too, that I have made etherization experiments with sartorius muscles acted on by 0.6-per-cent sodium-chloride solution, containing 0.02 to 0.06-per-cent $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$. I did not find, however, that the addition of the barium salt to the sodium-chloride solution increased the contracture-conditioning action of the latter on the sartorius. In some cases, indeed, the opposite effect seemed to be produced. Etherization produced in these experiments also its typical effect (Plate XXVIII, Fig. 6).

III. THE ACTION OF ETHER ON DEHYDRATED MUSCLES.

The remarkable effect on frog's voluntary muscle of local pressing, of drying by exposure to air, and of abstraction of water by means of glycerin injected into the animal's dorsal lymph sac have been described by Kuehne,† Biedermann,‡ and Langendorff# respectively. That diminution of the fluid content of the muscular tissue

* Ringer, *op. cit.*, p. 305.

† Kuehne, *Zeitschr. f. Biol.*, xxiv, 383, 1888, xxvi, 203, 1890.

‡ Biedermann, *Wiener Sitzungsab.*, xevii (3), 145, 1888. See also Grünhagen, Funke's *Lehrbuch der Physiologie*, 6 Aufl., i, 679, Leipzig, 1876.

Langendorff, *Arch. f. (Anat. u.) Physiol.*, 1891, 480.

is the essential common factor in the three cases is in the highest degree probable.* Of the two most striking features presented by such muscles, true secondary excitation of muscle by muscle, and response to simple stimulations by violent spasms of long duration, essentially analogous to those conditioned by veratrine and salt solution, the latter is of importance here. I have thought it worth while to investigate the effect of etherization on the form of contraction of sartorius muscles of curarized frogs into whose dorsal lymph sacs 1 to 2 cubic centimetres of glycerin had been injected an hour to an hour and a half before the preparation of the muscles.

The experiments were conducted in exactly the way before described in the case of veratrinized muscles.

Langendorff has already published graphic records of the prolonged spasmodic contractions of the muscles of glycerined frogs in response to single stimulations. I will only add to his account that these muscles show not only in their great tendency to this form of contraction, but also in other respects, a great general similarity in their behaviour to that of pressed muscles which Kuehne has so well described. It is often difficult to find a minimal strength of stimulus in the ordinary sense of the expression, the first contraction given by the muscle in response to single induction shocks gradually increasing in strength (e. g., the secondary coil being moved up by half centimetres from a distance of 40 to 30 centimetres from the primary) being a maximal prolonged spasm. Again, if a truly minimal strength of stimulus can be found, a stimulus a very little stronger usually gives rise to a maximal spasm, contractions intermediate in character not being obtainable. A weak stimulus which has elicited such a maximal spasm if repeated may produce no effect whatever, or evoke a comparatively simple twitch somewhat more prolonged in duration than normal. After a maximal spasm has been called forth by a make-shock of moderate strength, the corresponding break-shock may only cause such a twitch, although this merely apparent exception to the general rule of the greater efficacy

* Cf. Biedermann, *Electrophysiologie*, pp. 366-367, Jena, 1895.

of break-shocks for the production of contracture * is by no means a usual occurrence with the muscles of glycerined frogs.

The spasmodic contractions caused by even strong break-shocks repeated at intervals of one to two minutes vary very much in duration, and often also in amount.

From all this it would seem as though the affection of the muscle which conditions the appearance of contractures were less stable than is the case with veratrinized muscles.

Corresponding with these results it is found that, although ether does away with contracture, normal twitches making their appearance at a certain stage of its action, the cessation of etherization is not usually followed by the reappearance of contractures, as is the rule with veratrinized muscles, and with those treated with 0.6-per-cent sodium-chloride solution. What profound etherization often does for a veratrinized muscle moderate etherization effects for the muscles of glycerined frogs.

The action of ether on the form or contraction of such muscles is well shown in Figs. 7, 8, and 9 (Plates XXIX and XXX).

IV. DISCUSSION OF RESULTS.

After the results obtained from the action of ether in the case of agents so different in their nature as veratrine, physiological salt-solution, and dehydration, there can be but little doubt that, associated with the marked effect of ether on muscular contractility, there is a specific action on contracture in general, contracture disappearing sooner than contractility. How is this to be interpreted?

At the present time, when Grützner's doctrine of the composition of most muscles, at any rate, by fibres of two kinds, differing in their characteristic forms of contraction as in other ways, is being generally accepted, one is obliged to regard the action of ether on contracture from this standpoint, especially as Biedermann * has

* Cf. Tiegel, *Arch. f. d. ges. Physiol.*, xiii, 71, 1876; and Locke, *ibid.*, liv, 501, 1893.

† Biedermann, *Wiener Sitzungsber.*, xcii (3), 149, 1885; cf. also his *Electrophysiologie*, p. 93, Jena, 1895.

suggested that an explanation of the dicrotic form of contracture might be found in the composition of ordinary muscles by two kinds of fibres, and Overend,* discussing the subject more recently at some length, regards the alterations of the normal muscle-curve produced by veratrine as being little more than exemplifications of Gruetzner's view, the action of the poison on the "red" slowly acting muscle fibres being supposed to preponderate.

Since, however, the twitch of the "red" fibres, though of longer duration than that of the "white," is not of longer duration (of shorter, in fact, owing to the smaller latent period of the "white" fibres) than is the twitch of the whole muscle, in which both kinds of fibres take part, it is evident that the main problem of contracture—the enormous prolongation of the contracture in response to a single stimulation—remains untouched, whether it be called an affection of the "red" fibres, of the "white" fibres, or of both.†

The question, nevertheless, remains whether a real explanation is afforded by Gruetzner's doctrine of the dicrotism so often found more or less marked in contracture curves.

Awkward at the start are the dicrotic curves in which the notch after the first summit reaches or sinks below the abscissa, the succeeding recontraction, too, sometimes taking place after a distinct interval. Such curves have been noticed by Brunton and Cash, by Mendelssohn, and by Overend himself. To reconcile these with the attempted explanation it seems to me necessary to assume that the inertia of the falling muscle lever and load gained during the relaxation of the quickly acting "white" fibres overcome the contraction of the slowly acting "red" fibres, which must have already commenced unless veratrine,

* Overend, *Arch. f. exp. Path. u. Pharm.*, xxvi, 1, 1890.

† It may be here pointed out that the same consideration holds good in the case of the lengthening of the duration of the simple twitch of a muscle produced by fatigue. Overend (*op. cit.*, p. 17) attempts to explain it by the earlier exhaustion of the "white" fibres. It is, however, obvious that, if this be granted, the *absolute* lengthening in duration of the simple twitch by fatigue—i. e., not merely apparent owing to the lessening of the height of contraction (cf. Marey, *Du mouvement dans les fonctions de la vie*, p. 340, Paris, 1868; and Volkmann, *Arch. f. d. ges. Physiol.*, iii, 374, 1870)—is as mysterious as ever.

while shortening the latent period of the relaxed whole muscle (Mendelsohn), lengthens enormously the latent period of the relaxed "red" fibres in it.

In most curves of the kind in question the inertia of weight and lever is shown to be at work by the overextension of the muscle in its first relaxation immediately recovered from by its own elasticity (cf. Fig. 10, Plate XXX). Overend's curves, however, obtained with Marey's spring myograph on a drum revolving horizontally, show no signs of such inertia oscillations, and render it probable that a veratrinized muscle can entirely relax after its first twitch before the "after-action" commences. But, if this be so, "red" and "white" fibres fail utterly to explain dicrotism, the more so since Overend himself concluded, from experiments on the rabbit's "red" soleus, that its latent period was shortened by veratrine.

If the dicrotic were the only anomalous form of contracture curve requiring special explanation, one might be tempted, in spite of the difficulties just raised, to still seek to explain it by the existence of two classes of fibres in voluntary muscle. Such is, however, by no means the case, even with veratrine alone. Veratrine curves may possess three well-marked summits, as Overend himself saw, or the second rise and fall of the curves may be broken by a whole series of more or less rhythmical contractions superposed on it. Such irregularities of contracture curves are much more marked in the case of other contracture-producing agents than with veratrine. Fig. 11, Plate XXX, is an example of this in the case of a curarized muscle acted on by physiological salt-solution. A special kind of fibre for each summit in a curve like this can hardly be assumed.

Lastly, the effects of increase of load and of repeated stimulation of the muscle are unfavorable to the application of Gruetzner's doctrine advocated by Overend. The "white" quickly acting fibres are held by all the advocates of the doctrine to be the more easily fatigued, and to be the weaker as far as the lifting of heavy loads is concerned. And yet, as Overend himself found, an increase of the load has more effect in lowering the secondary rise than it has in lowering the initial shortening of a veratrinized muscle—an effect

which I have also observed in the case of muscles acted on by physiological salt solution.* Again, the effect of repeated stimulation in causing the disappearance or marked diminution of all forms of contracture, the ordinary response of the muscle to a single stimulation being usually but little affected, does not harmonize with the view that contracture is especially the function of the fatigue-resisting "red" fibres.

Does now Gruetzner's doctrine afford an explanation of the effect of ether on contracture?

The ease with which it apparently does so is certainly fascinating. One has only to suppose that just as, according to Overend, the action of veratrine is more pronounced on the "red" fibres, the same is true for ether also, the "red" losing their contractility earlier than the "white" fibres. Unfortunately, however, there is in existence experimental evidence which precludes the drawing of this parallel.

It was found by Willy Neumann in Luchsinger's† laboratory, in the case of a great number of substances, including ether, that they uniformly produced their particular effects more speedily upon the more irritable, quickly contracting muscles than upon the less irritable, slowly contracting muscles. The differences in mechanical function between these muscles must be produced, if Gruetzner's doctrine be correct, all the fibres in each muscle not being alike, by the varying predominance of one or other class of fibres in them, and this same varying predominance must have produced the differences in respect to the action of poisons observed by Willy Neumann.‡ It

* Mendelssohn had also found that "le même effet" (diminution of the effect of veratrine on muscle) "est produit par l'augmentation de la charge, mais dans ce cas, il n'est pas persistant, et disparaît avec la diminution de la charge" (*Comptes rendus de la Soc. de Biol.*, 1883, 150). Since the above was written Schenck (*Arch. f. d. ges. Physiol.*, lxi, 505-508, 1895) has shown that the ratio of height of isometric contraction to height of isotonic contraction is much greater for the "Initialzuckung" than for the "Veratrinverkürzung." "Der Muskel ist in der Initialzuckung weniger dehnbar als in der Veratrinverkürzung."

† Willy Neumann, *Ueber toxicologische Verschiedenheiten functionell verschiedener Muskelgruppen*. Dissertation, Bern, 1883.

‡ Cf. Gruetzner, *Recueil zoologique Suisse*, i, 678, 1884.

may therefore be concluded that "white," quickly acting fibres are more easily affected by ether than the slowly acting "reds." If, then, there is only to be seen in the action of ether on the veratrinized sartorius a differentiation between "red" and "white" fibres, it must be concluded that the first summit of the dirotic curve which persists longer under the action of ether must be due to the activity of "red" fibres—a conclusion the reverse of that of Overend, but quite as lacking in any real experimental foundation. Such a conclusion, too, attributes to veratrine the property of reversing the normal contractile relations of the "white" and "red" fibres to one another, the contraction of the "white" becoming slow and prolonged in comparison with that of the "red," which is now relatively the quicker.

It seems to me, therefore, that no such ready explanation as the Gruetznierian doctrine seems at first to afford is available for the action of ether on contracture, and that ether must be regarded as having a specific action on contracture as such, be it of "red" or of "white" muscle fibres.

A second explanation of the action of ether on contracture which offers itself is based upon the assumption that its action on the muscle consists essentially in the change of a strong into a weak stimulus, the latter being unable to produce contracture.

This conception might be upheld in the case of the action of ether on the contracture of muscles treated with salt-solution, since, as a rule, relatively strong stimuli alone cause this form of contraction. It can not, however, hold good in the case of veratrinized muscles, in which minimal stimuli were always found to produce typical contractions, and this even after several strong stimulations sufficiently far apart (Plate XXVII, Figs. 1 and 3).

The action of ether, then, consists in something more than a mere reduction in strength of stimulus as ordinarily understood. While allowing at a certain stage of its action the occurrence of those metabolic processes on which a "twitch" depends, ether prevents the occurrence of those processes on which contracture depends.

What now are the processes on which contracture depends? An

answer to this question has recently been attempted by Schenck,* who supposes the persistent contractions conditioned by ammonia, veratrine, the constant current, spontaneous and heat rigor, and by certain seasonal conditions (Tiegel) to be all due to uncoordinated contractions of the contractile elements of muscle brought about by the inability of these forms of contraction to propagate themselves along the muscle in the normal wavelike manner. It may be possible that the mechanical and other peculiarities of these forms of persistent contractions are, as Schenck supposes, ultimately due to this lack of conductive propagation along muscle fibres, and in spite of the fact that etherization abolishes the conduction of excitation along muscle before it does away with local polar excitability,† it may be possible to reconcile Schenck's view with the fact that etherization suppresses contracture at an earlier period than the normal twitch of the muscle by supposing that, unless the process of excitation be first propagated along the muscle fibre, the local uncoordinated contractions incapable of conduction can not come into existence. What, however, causes these local uncoordinated contractions to follow the passage of a contraction wave through a veratrinized muscle Schenck's theory does not attempt to explain, although the similarity found by him in the mechanical characters of the persistent contractions conditioned by veratrine and by ammonia, the classical chemical stimulus of muscle, is in favour of the probability of a conception which I have long entertained, and which, I think, expresses some, at any rate, of the truth.

With the exception of the unknown seasonal and nutritional conditions which bring about the contracture of Kronecker and Tiegel, I do not know of any agency or substance which conditions contracture in general that is not known to be capable of producing stimulation of muscle itself or of its motor nerve endings. The kind of stimulation in question is that of the agencies described by Biedermann,‡ which "stimulate without killing," in contradistinction to those

* Schenck, *Arch. f. d. ges. Physiol.*, lxi, 494, 1895.

† Biedermann, *Wiener Sitzungsber.*, xcvi (3), 98, 1888.

‡ Biedermann, *Ibid.*, lxxxii (3), 275, 1880.

chemical stimuli of muscle which had been alone recognized by Hermann,* and "locally strongly impair excitability, and, if their action be sufficiently prolonged, destroy it." The former have, so to speak, a chronically stimulating action in contradistinction to the acutely stimulating influence of substances, such as acids and potassium salts, which soon put an end to irritability. May not then the condition of chronic minimal or latent irritation be causally associated with contracture? The increase of excitability caused especially by a strong stimulus,† and known to persist for a considerable time, might make the feeble continuous excitation by the chemical stimulus, which was previously nearly or entirely inefficacious, now capable of marked effect, so that it evokes the various forms of more or less persistent after-contraction. The action of ether is on this hypothesis readily explained, the lowering of excitability caused by it being able to render the feeble more or less latent continuous stimulation incapable of becoming actual long before contractility to strong stimulation is abolished.

Further discussion of the many indirect evidences which favour this view I do not care now to indulge in, but hope to return to the subject later and deal with it in the light of the results of direct experimental evidence.

REGARDING POSITIVE KATHODIC POLARIZATION OF VERTEBRATE VOLUNTARY MUSCLE.

Although this subject may appear at first sight to be far removed from the action of ether on contracture, it will become evident that the experimental results above described have established a distinct connection between them.

In 1885 Biedermann published experiments on the sartorius of the frog in proof of the existence of positive kathodic polarization of striated muscle.‡ His method was to veratrinize by local applica-

* Hermann, *Handbuch der Physiologie*, Bd., i (1), p. 105, Leipzig, 1879.

† Cf. Buckmaster, *Arch. f. (Anat. u.) Physiol.*, 1886, 472.

‡ W. Biedermann, *Wiener Sitzungsber.*, xcii (3), 142, 1885.

tion the tibial end only of the frog's sartorius, and then, after an immersion of the whole muscle for from fifteen to thirty minutes in physiological salt solution, to pass through it for a moment from pelvic to veratrinized tibial end the current of two Daniell's cells. Immediately after the breaking of this current the middle of the muscle and its tibial end are connected through a galvanometer, which shows a strong current passing through it from middle to tibial end, due to the local intense and prolonged excitation of the latter due to its veratrinization. This powerful action current is rapidly compensated so as to bring the galvanometer back to zero, and, after first opening the galvanometer circuit, the battery current is again passed through the muscle for one or two seconds in the same descending direction as before. The galvanometer is immediately afterward again connected with the muscle, and now shows a current passing through it from tibial end to muscle middle. The effect of the second passage of the battery current has therefore been to lessen the action current caused by the first passage of it, so that either the middle of the muscle has become more negative or the tibial end more positive. Biedermann held the latter to be the case, and explained the increased positivity of the tibial end as being due to an active inhibitory reaction which occurs at the kathode at break—a reaction opposite in nature to the well-known excitatory action of the kathode at make. Since the galvanometric effect observed indicates a current in the kathodic half of the muscle in the same direction as the battery current which brought it into existence, it was called, in accordance with Hering's nomenclature, a positive kathodic polarization.

Biedermann was able to get similar galvanometric after-effects with unpoisoned muscles, especially after killing their kathodic tibial ends. These effects he similarly interpreted as due to the kathodic muscle substance being left electrically more positive after the passage of a strong constant current of short duration, in consequence of a reaction at break against the kathodal excitation at make.

Working in 1891 in Hering's laboratory, in which Biedermann had also made his experiments, I found that electrical effects analo-

gous to those described by him could be produced by merely stimulating with induction shocks the pelvic end of the sartorius, the tibial end of which had been locally veratrinized in accordance with Biedermann's method.

The induction shocks were led through platinum electrodes close together, and close to the pelvic end of the muscle, the middle and tibial end of which were connected with the galvanometer. The first shock sent into the muscle caused a strong action current, due to the persistent negativity of the veratrinized tibial end. This being rapidly compensated, a second induction shock caused a marked diminution in the strength of this action current, the negativity of the tibial end having been apparently considerably diminished. If, now, Biedermann's method and conclusions were reliable, this effect indicated that an inhibitory after-action of stimulation was conducted to the tonically contracted tibial end along the muscle from the pelvic end—a discovery of some importance, the possibility of which had indeed been referred to by Biedermann himself.

It is obvious, however, that the accuracy of such interpretations of Biedermann's and my own observations depend absolutely on the change of potential indicated by the galvanometer being an increased positivity of the veratrinized tibial end, and not an increased negativity of the middle of the muscle, which would also produce the effect in question.

Following Biedermann's method of poisoning the sartorius, I had, after immersing the tibial end for a few minutes in a dilute veratrine solution, placed the whole muscle for from fifteen to thirty minutes in physiological salt solution. Control experiments now showed that such a muscle, after the destruction of the whole of its veratrinized lower end with a hot glass rod, gave an enormously greater negative variation when stimulated with a single induction shock than can be obtained from an ordinary muscle. Further experiments showed that previous veratrinization was not, as might have been supposed, necessary for the production of this result, but that immersion of the muscle in pure salt-solution was by itself sufficient to produce the effect, which was found myographically to be associated with a contracture-

conditioning action of a 0.6-per-cent solution of sodium chloride, an action analogous to that of veratrine, but not so marked.*

The effects, therefore, which had been observed by Biedermann and myself may have been simply due to greatly increased negativity of the muscle middle, rendered possible by the action of the salt-solution. In fact, in the polarization experiments which I was able to make in control of Biedermann's positive kathodic polarization of normal muscle not locally veratrinized, such a polarization was always much more easily obtained with muscles treated with salt-solution than with muscles not so treated.†

The subject was therefore in need of a thorough revision, which, however, it has not yet received. Biedermann, in his recently published "Electrophysiologie" (pp. 386-391), states merely that he has convinced himself that positive kathodic polarization can occur in normal muscles not locally veratrinized that have not been treated with salt-solution, and gives his old results with locally veratrinized muscles without comment, although, for the reasons already given, they are, in a very high degree, untrustworthy.

It may be here pointed out that experiments made without the use of a normal solution with which the muscle can be kept moist, must be regarded, unless a moist chamber is employed, as by no means free from the possibility of error, inasmuch as the progressive drying of the muscle may condition a prolongation and intensification of excitation analogous to that conditioned by salt-solution.

It is useless too to lay stress, as Biedermann does, on the tendency to a "*polares Versagen*," the inability of currents leaving the muscle through a locally killed or contracted part of it to excite it. There are too many conditions in actual practice tending to prevent this "*polares Versagen*," ‡ for its existence to be assumed in experiments in which it is not demonstrated, and no experiment has hitherto been published in which it was shown that a positive kathodic polarization was unaccompanied by an abnormally intensified contraction of the muscle.

* F. S. Locke, *Arch. f. d. ges. Physiol.*, liv, 501, 1893.

† F. S. Locke, *op. cit.*, p. 517.

‡ Cf. F. S. Locke, *op. cit.*, p. 521.

The question of the action of ether on positive kathodic polarization can now be considered. Biedermann * has himself investigated the effect of etherization on the secondary electromotive properties of muscle, and the comparison of his results obtained with the galvanometer with the myographic observations that have been described in this communication is worth making. Biedermann found that in those cases in which he observed positive kathodic polarization it always disappeared under etherization at a time at which the muscle still twitched in response to the make of the battery current. The three other varieties of secondary electromotive phenomena, not only negative kathodic and positive anodic polarization, which are due to the make kathodic and break anodic excitations respectively, but also negative anodic polarization analogous to which in its inhibitory and assimilatory character Biedermann considers positive kathodic polarization to be—all these persist under complete etherization of the muscle. Such a difference in behaviour can scarcely be explained from Biedermann's standpoint, but is at once comprehensible in the light of the myographic results, if positive kathodic polarization be nothing more than the galvanometric expression of the enormous action currents accompanying contracture.

EXPLANATION OF MUSCLE TRACINGS.

PLATES XXVII-XXX.

Large Leclanché cells coupled up in multiple arc two abreast were used to supply the primary coil of the stimulating Du Bois inductorium.

The crosses (X X) indicate the period of etherization. In the case of curves arranged in "*imbrication latérale*," a cross indicates between which two stimulations etherization was begun or ended. In the case of muscles stimulated surrounded by fluid, a cross indicates when the solution containing ether is turned on or off: in these experiments the curves are, conventionally regarded, inverted.

All curves read from left to right.

PLATE XXVII.

Fig. 1A.—Fresh curarized and veratrinized sartorius stimulated by weak break-shock at commencement of experiment.

* Biedermann, *Wiener Sitzungsber*, xcvi (3), 84, 1888.

Fig. 1B.—The same muscle stimulated every 85.5 to 86.5 seconds with a strong break-shock (distance of secondary from primary, 0 centimetre. 2×2 Leclanché). Time-marker writes seconds. Load, 80 ($\div 13.5$) grammes.

Fig. 2.—Curarized and veratrinized sartorius stimulated every 130.5 to 131.5 seconds with a strong break-shock (distance of secondary coil from primary, 0 centimetre. 2×2 Leclanché). Load, 65 ($\div 13.5$) grammes. Time-marker writes seconds. This figure is reduced to four fifths of its original size.

Fig. 3A.—Fresh curarized and veratrinized sartorius stimulated with weak break-shock (distance of secondary from primary, 18 centimetres. 2×2 Leclanché).

Fig. 3B.—The same muscle stimulated every 81 to 82 seconds with a strong break-shock (distance of secondary from primary, 0 centimetre). Time-marker writes seconds.

Fig. 3C.—The same muscle stimulated, after the completion of Fig. 3B, by a weaker break-shock (distance of secondary from primary, 9 centimetres). Load, 80 ($\div 13.5$) grammes.

PLATE XXVIII.

Fig. 4A.—Fresh uncurarized sartorius, surrounded by Ringer's solution, stimulated with strong make- and break-shocks (distance of secondary from primary, 0 centimetre. 4×2 Leclanché). Muscle unloaded (i. e., so lightly loaded as just to be able to return to the abscissa). Time-marker writes intervals of three seconds.

Fig. 4B.—The same muscle, after having been surrounded by 0.6-per-cent NaCl solution for twenty minutes. It is being stimulated every two minutes with a break-shock of the same strength as in Fig. 4A.

Fig. 4C.—The same muscle at a later stage of the experiment, rhythmical stimulation and the stream of salt-solution having been kept up. The stimulation here took place eight minutes later than the last in Fig. 4B.

Fig. 5A.—Curarized sartorius in Ringer's solution, containing 0.02-per-cent curare, and stimulated with strong make- and break-shocks (distance of secondary from primary, 0 centimetre. 4×2 Leclanché). Muscle unloaded. Time-marker writes intervals of ten seconds.

Fig. 5B.—The same muscle, after having been surrounded with 0.6-per-cent NaCl solution, containing 0.02-per-cent curare, for twenty minutes, without being stimulated electrically, the commencement of rhythmical stimulation (a break-shock of the same strength as in Fig. 5A, every two minutes) being shown here. The temperature in this experiment varied between 15.2° and 15.4° C. Figs. 5A and 5B have been reduced to two thirds of their original size.

Fig. 6.—Curarized sartorius in 0.6-per-cent NaCl solution, containing 0.06-per cent $\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$ and 0.02-per-cent curare for twenty-three minutes before commencement of etherization, and stimulated eight times at intervals of sixty seconds with a strong break-shock (distance of secondary from primary, 0 centimetre. 5×2 Leclanché) before the first similar stimulation shown in the part of the tracing reproduced. Muscle unloaded. Time-marker writes intervals of sixty seconds.

PLATE XXIX.

Fig. 7.—Curarized sartorius of glycerined frog stimulated every 113.5 to 114.5 seconds by a strong break-shock (distance of secondary from primary, 5 centimetres. 2×2 Leclanché). Load, 40 ($\div 13.5$) grammes. Time-marker writes seconds.

Fig. 8.—An experiment similar to that of Fig. 7, except that the muscle was stimulated every 137 to 138 seconds.

PLATE XXX.

Fig. 9.—Curarized sartorius of a glycerined frog stimulated with a strong break-shock (distance of secondary from primary, 0 centimetre. 2×2 Leclanché) every 120 to 121 seconds. Load, 60 ($\div 13.5$) grammes. Time-marker writes seconds.

Fig. 10.—Uncurarized sartorius after an immersion for an unrecorded time in 0.6-per-cent NaCl solution. Poor pale muscle. Load, 20 ($\div 13.5$) grammes. Time-marker writes seconds. The muscle had been previously stimulated a few times. The effect of an ascending break-shock (distance of secondary from primary, 0 centimetre) is shown in the figure.

Fig. 11.—Curarized sartorius after an immersion for ten minutes in 0.6-per-cent NaCl solution. Stimulated by an ascending break-shock (distance of secondary from primary, 0 centimetre. 3×2 Leclanché). Time-marker writes seconds. The corresponding make-shock had produced a contracture as marked but more regular. Temperature of laboratory and of the salt-solution 21.1° C.

In the case of Figs. 10 and 11 the same muscle lever and moist chamber were used as in the case of Figs. 1, 2, and 3.

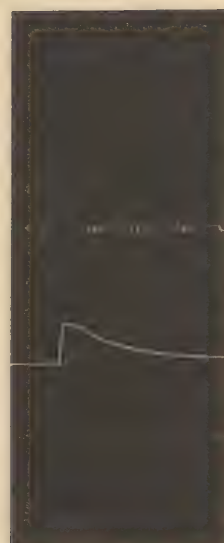


FIG. 1.



FIG. 2.

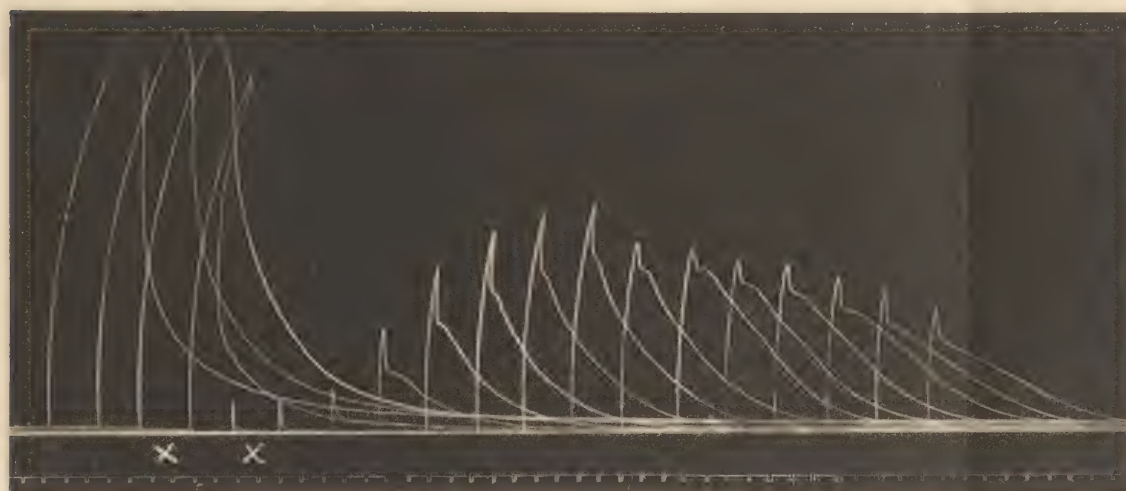


FIG. 3.

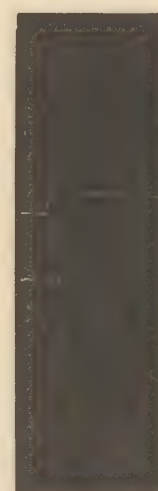


FIG. 4.

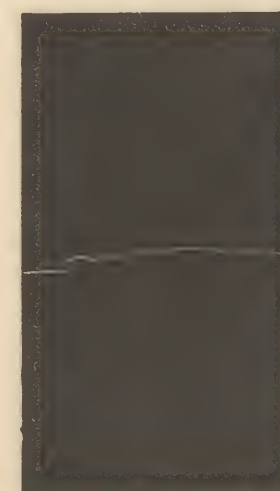


FIG. 5.

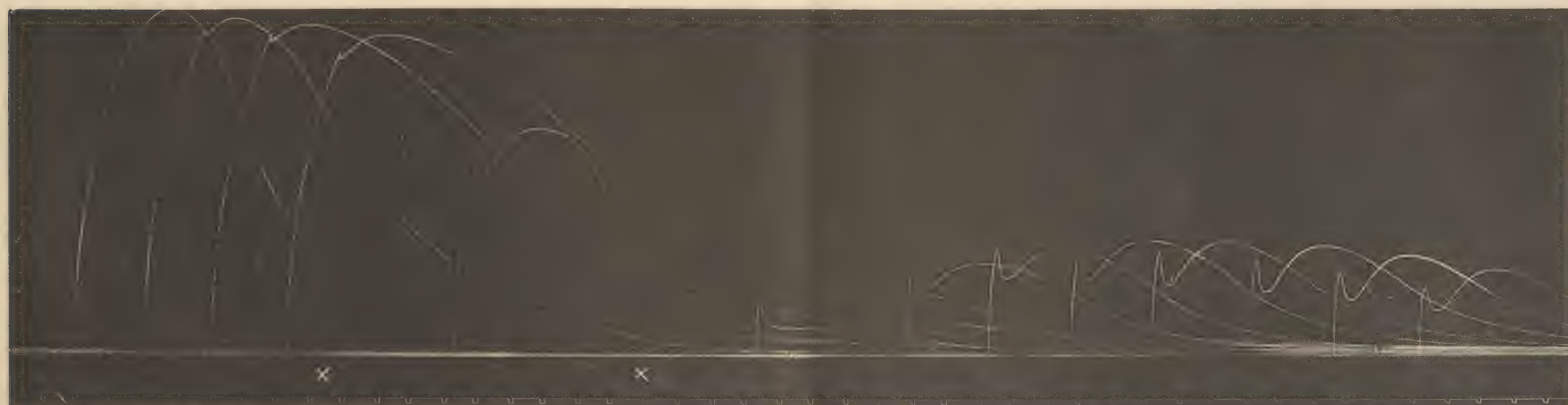


FIG. 6.

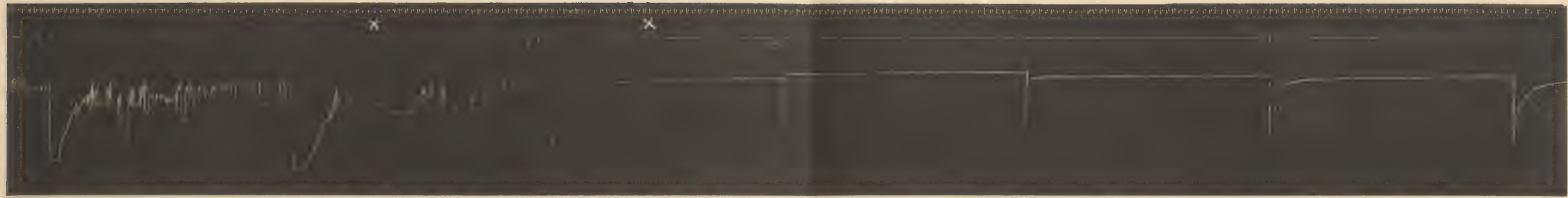


FIG. 4 B.



FIG. 4 A.

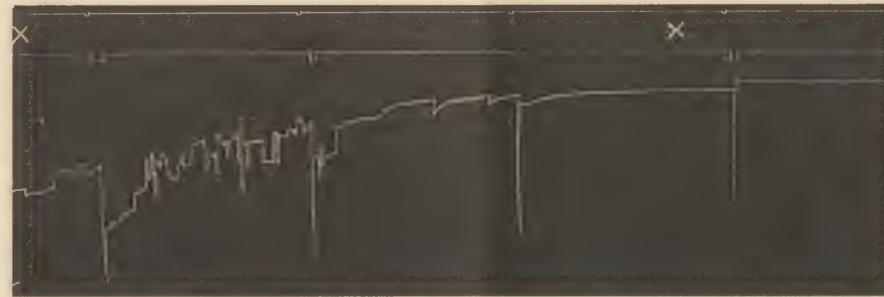


FIG. 5.

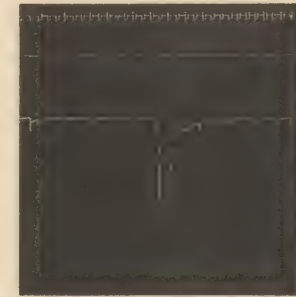


FIG. 4 C.

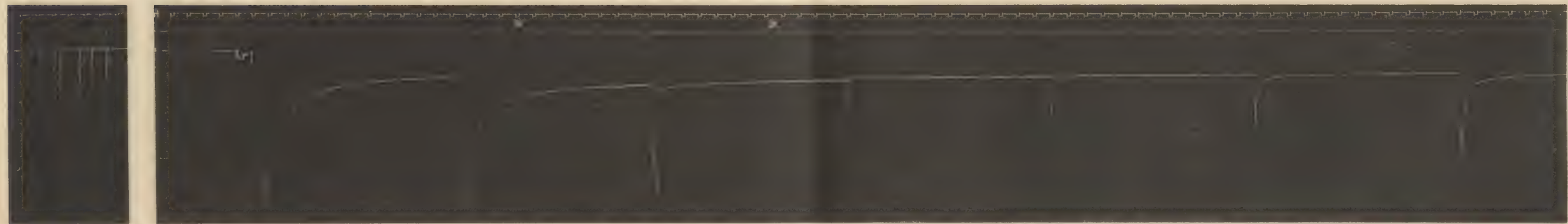


FIG. 5 A. (2-9)

FIG. 5 B. (2-9).

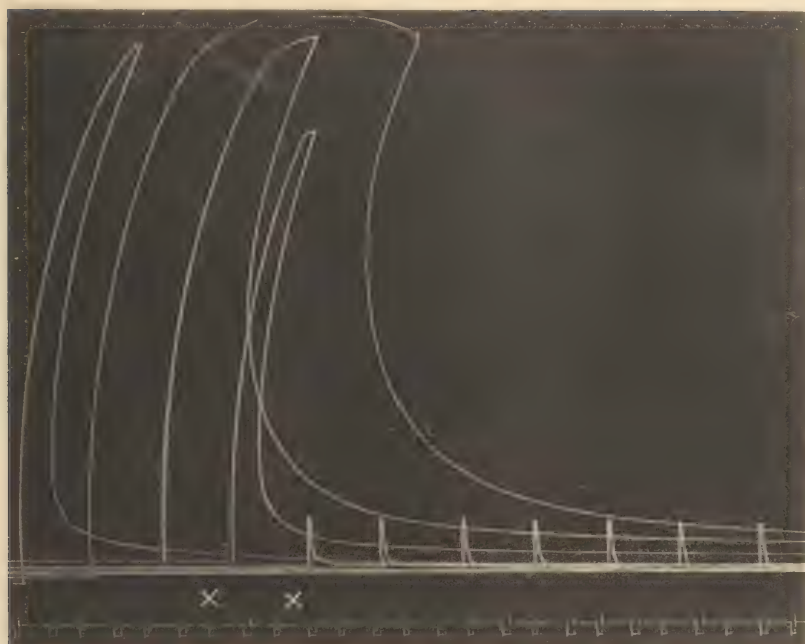


FIG. 7.

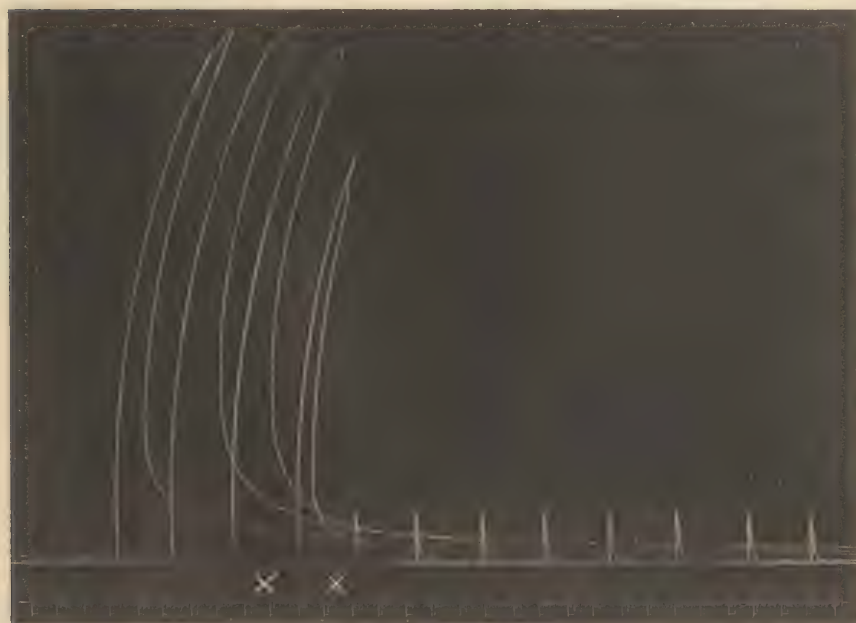


FIG. 8.

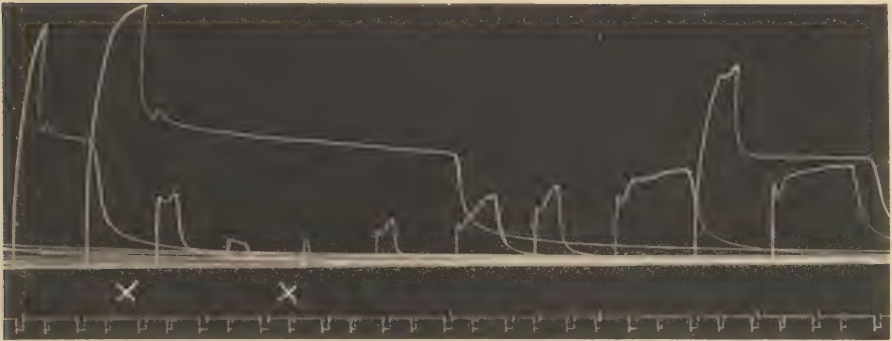


FIG. 9.



FIG. 10.



FIG. 11.

